EPHA2 AGONISTS AND USES THEREOF

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/682,079, filed Jun. 7, 2018, and U.S. Provisional Application No. 62/718,267, filed Aug. 13, 2018, which are incorporated herein by reference in their entirety and for all purposes.

STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY SPONSORED RESEARCH AND DEVELOPMENT

[0002] This invention was made with government support under grant no. CA168517 awarded by the National Institutes of Health. The government has certain rights in the invention.

REFERENCE TO A "SEQUENCE LISTING," A TABLE, OR A COMPUTER PROGRAM LISTING APPENDIX SUBMITTED AS AN ASCII FILE

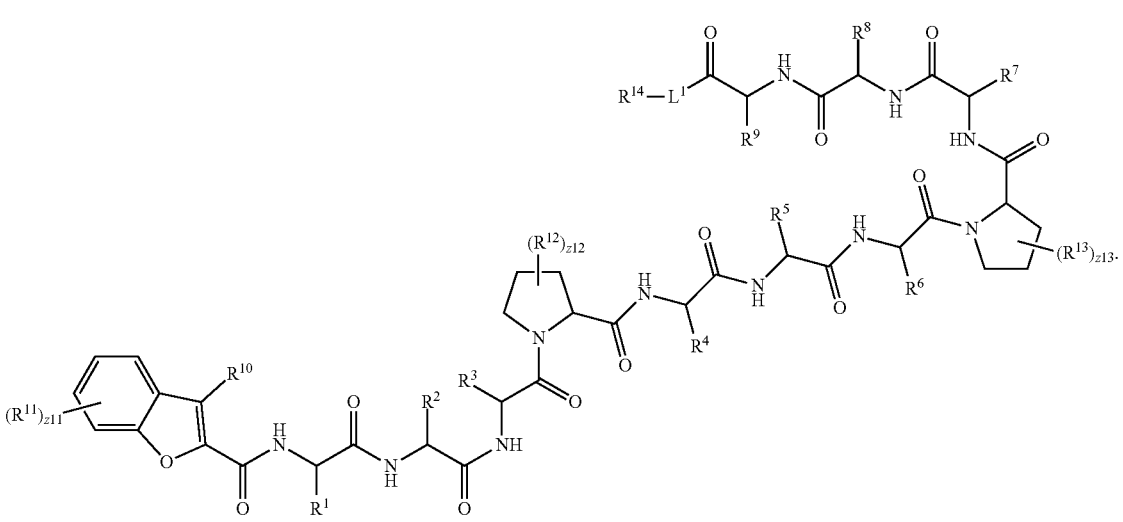
[0003] The Sequence Listing written in file 054156-503001WO_Sequence_Listing_ST25.txt, created Jun. 7, 2019, 35,287 bytes, machine format IBM-PC, MS Windows operating system, is hereby incorporated by reference.

BACKGROUND

[0004] EphA2 belongs to a class of receptor tyrosine kinases that have been implicated in tumorigenesis, drug resistance, and metastatic behaviors of several solid tumors including prostate cancer, melanoma, urinary bladder, breast, ovarian, pancreatic, brain, esophagus, lung, and stomach cancers, and leukemia. In cancer cells, the unbalanced overexpression of the receptor compared to its ligands (ephrin-A) primes the EphA2 pro-oncogenic activity. Hence, deriving novel and more potent EphA2 binding agents that displayed a nanomolar affinity for the receptoris needed. Described herein, inter alia, are solutions to these and other problems in the art.

BRIEF SUMMARY OF THE INVENTION

[0005] In an aspect is provided a compound having the formula:



(I)

[0006] R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 are each independently hydrogen, halogen, —CCl_3, —CBr_3, —CF_3, —CI_3, —CH_2Cl, —CH_2Br, —CH_2F, —CH_2I, —$CHCl_2$, —$CHBr_2$, —CHF_2, —CHI_2, —CN, —OH, —NH_2, —COOH, —$CONH_2$, —NO_2, —SH, —SO_3H, —SO_4H, —SO_2NH_2, —$NHNH_2$, —ONH_2, —$NHC(O)NHNH_2$, —$NHC(O)NH_2$, —$NHSO_2H$, —NHC(O)H, —NHC(O)OH, —NHOH, —$OCCl_3$, —$OCBr_3$, —OCF_3, —OCI_3, —OCH_2Cl, —OCH_2Br, —OCH_2F, —OCH_2I, —$OCHCl_2$, —$OCHBr_2$, —$OCHF_2$, —$OCHI_2$, an amino acid side chain, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^1 and R^5 may optionally be joined to form L^2; R^9 and the nitrogen atom adjacent to the carbon to which R^9 is attached may optionally be joined to form a substituted or unsubstituted heterocycloalkyl. L^2 is a covalent linker. R^9 is an amino acid side chain, bioconjugate reactive moiety, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. R^{10} is hydrogen, halogen, —CCl_3, —CBr_3, —CF_3, —CI_3, —$CHCl_2$, —$CHBr_2$, —CHF_2, —CHI_2, —CH_2Cl, —CH_2Br, —CH_2F, —CH_2I, —CN, —OH, —NH_2, —COOH, —$CONH_2$, —NO_2, —SH, —SO_3H, —SO_4H, —SO_2NH_2, —$NHNH_2$, —ONH_2, —$NHC(O)NHNH_2$, —$NHC(O)NH_2$, —$NHSO_2H$, —NHC(O)H, —NHC(O)OH, —NHOH, —$OCCl_3$, —OCF_3, —$OCBr_3$, —OCI_3, —$OCHCl_2$, —$OCHBr_2$, —$OCHI_2$, —$OCHF_2$, —OCH_2Cl, —OCH_2Br, —OCH_2I, —OCH_2F, —N_3, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted het-